**Attorney Docket No.: 0492611-0383/MIT9015**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| Applicant: | Madry, *et al.* | Examiner: | Katcheves, Konstantina |
| Serial No.: | 09/809,456 | Art Unit: | 1636 |
| Filing Date: | March 15, 2001 | | |
| Title: | TISSUE ENGINEERING ENHANCED BY THE TRANSFER OF A GROWTH FACTOR GENE | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

**DECLARATION UNDER 37 C.F.R. 1.132**

I, Gordana Vunjak-Novakovic, Ph.D., declare as follows:

1. I received a doctorate in Chemical Engineering from the University of Belgrade in 1980.

2. I was a professor of chemical engineering at the University of Belgrade from 1981 through 1993. During that time I was awarded a Fulbright Fellowship for the 1986-1987 school year.

3. From 1993 to 1998 I was a research scientist at the Massachusetts Institute of Technology (MIT). During this time, I was also responsible for scientific oversight over the design and testing of the cell culture system for the International Space System. I was awarded "Paper of the Month" for papers appearing in the American Institute of Chemical Engineering Journal in July 1994 and March 1996.

4. Since 1998 I have been a Principal Research Scientist in the Division of Health Sciences and Technology at MIT. I am also an adjunct professor in the Department of Bioengineering at Tufts University, a position I have held since 1994.

5. In 2000, I was made a fellow of the American Institute for Medical and Biological Engineering.

6. I am an author of a number of articles and book chapters relating to tissue engineering, cell culture, and *in vitro* cell cultivation and tissue synthesis. A list of some of these is included in the Appendix.

7. As a result of my general background, knowledge, and experience with tissue engineering and *in vitro* cell cultivation, I offer the following statements and opinions:

A. Chondrocytes produce collagen type II, the predominant component of articular cartilage. This collagen is chemically and structurally different from collagen type I, which is found in bone, skin, and other organs. Collagen type I is produced by cells such as osteoblasts and fibroblasts.

B. Chondrocyte phenotype is dependent on environment. These cells will continue to produce collagen type II and other extracellular matrix components of cartilage so long as they experience the chemical and mechanical environment typical of healthy articular cartilage.

C. If the environment experienced by chondrocytes is modified, then they often exhibit a phenotype more typical of fibroblasts than of chondrocytes. They produce collagen type I instead of collagen type II. Histologically, they exhibit the flat shape typical of fibroblasts rather than the round morphology of chondrocytes.

D. For this reason, it is difficult to culture chondrocytes *in vitro*. Chondrocytes cultured on stan dard tissue culture substrates (such as tissue culture plastics) quickly revert to fibroblastic phenotypes.

6. All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents issued thereon.

Gordana Vunjak-Novakovic, Ph.D.

9/8/04

Date

## Appendix


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